REMARKS

Claim Status

Claims 6, 7, 19-26, 31 and 33 are cancelled. Of these, claims 19-26 are cancelled as being drawn to unelected subject matter – this cancellation is made without prejudice to pursuing the subject matter of these claims in a divisional application.

Claims 13, 34 and 43-48 are withdrawn for reciting unelected subject matter. Pursuant to the examination guidelines regarding restriction practice and generic claims (MPEP § 809), Applicants will seek to rejoin these claims if claim 1 is deemed allowable. Claim 1 serves as a linking claim for reciting the generic term "non-standard amino acid degrading protein" – the withdrawn claims recite various species of this element that are shown in the instant application to effect the reduction of non-standard amino acid (NSAA) incorporation in a heterologously expressed protein.

Claims 43-48 are new, and are supported by the original claims.

Claims 1-5, 9, 10, 17, 27-29, 32, 34, 36-38 and 42 are currently amended. Most of the amendments remove non-elected subject matter. Other amendments to the claims are made for clarification and formalization purposes, or to correct typographical errors.

Applicants respectfully submit that the foregoing amendments to the claims do not introduce any new subject matter to the application. With the present amendments, there are thirty-six claims pending for examination, namely claims 1-5, 8-18, 27-30, 32 and 34-48.

Restriction Requirement

The Examiner alleges that the instant application claims multiple different inventions and therefore issues a restriction requirement. These inventions are listed in the Office Action as follows:

I. "[A] method for reducing the incorporation of non-standard amino acids into a heterologous protein by using a microorganism expressing (1) at least one heterologous protein...and (1) at least one non-standard amino acid degrading protein" (original claims 1-18 and 41).

II. "[A]n *E. coli* glutamate dehydrogenase protein comprising a lysine 92 to leucine variation or an E. coli glutamate dehydrogenase having the sequence of SEQ ID NO:4" (original claims 19-20).

III. "[A] polynucleotide encoding the glutamate dehydrogenase of Group II and cell comprising said polynucleotide and a method of isolating a protein using a cell expressing 1) at least one heterologous protein...and (1) at least one non-standard amino acid degrading protein (original claims 21-41).

The examiner additionally requires the election of (i) a polynucleotide sequence encoding a particular somatotropin and (ii) a particular NSAA degrading protein. Judging from this restriction and the language of the original claims, Applicants kindly note that the Examiner may have actually meant to include claim 42 in Group I instead of claim 41. Applicants take this apparent discrepancy into account with the instant response.

With traverse, Applicants elect the method of group I that employs polynucleotides encoding bovine somatotropin (the "heterologous protein") and wildtype glutamate dehydrogenase (GDH, SEQ ID NO:2) (the "NSAA degrading protein"). SEQ ID NO:1 is an example of a polynucleotide that encodes this GDH. Since the genetic code is degenerate, multiple different polynucleotides can express the same protein; for this reason, the elected invention should not be restricted to any particular polynucleotide sequences. Claims 1-5, 8-12, 14-18 and 42, as currently pending, read on this elected grouping of subject matter.

Certain aspects of the present restriction requirement are traversed as follows. Firstly, Applicants respectfully submit that the requirement to elect a specific somatotropin as the heterologous protein should be withdrawn. The crux of the elected invention is not related to the heterologous protein expressed, but rather the provision of a NSAA degrading enzyme to effect the production of proteins having reduced incorporation of NSAA. Skilled artisans would readily acknowledge that the elected method is applicable to preventing the incorporation of NSAA in any heterogously expressed protein, not just somatotropin. Hence, if the Patent Office limits it search of the method to a particular heterologous protein, the real essence of the invention would not have received an adequate examination.

Further regarding the traversal, Applicants respectfully submit that the non-cancelled/non-withdrawn claims of group III (27-30, 32, 35-41) should be examined along with the claims of group I. At their basic level, the remaining group III claims only differ from the group I claims by additionally reciting the isolation of the heterogously expressed protein; both these claims sets share the step of co-expressing a heterologous protein with a NSAA degrading protein. These claim sets are therefore not mutually exclusive. Because of this non-exclusivity and that the methods of these claim sets are related, the restriction requirement between claims 27-30, 32, and 35-41 and the group I claims should be withdrawn.

Lastly regarding the restriction requirement, Applicants respectfully submit that the claims should be examined for the method as it employs wildtype GDH (SEQ ID NO:2) or K92L GDH (SEQ ID NO:4). Except for residue position 92, the amino acid sequences of these NSAA degrading proteins are completely identical. Furthermore, the wildtype and K92L GDH proteins show similar activity in blocking the incorporation of the NSAA norleucine in a heterologously expressed protein (refer to the second and third rows of Table 5 in the original specification).

This high level of similarity – both structural and functional – renders these GDH's as non-distinct from each other; thus, the Patent Office would be able to search both these proteins without any extra burden.

Since claim 2 recites the generic term "glutamate dehydrogenase," it serves as a linking claim as per MPEP § 809. Therefore, should the restriction requirement between the wildtype and K92L GDH proteins be maintained, Applicants will seek to rejoin the K92L GDH subject matter if claim 2 is deemed allowable. .

The above remarks notwithstanding, Applicants reserve the right to file one or more divisional applications to protect non-elected inventions.

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Respectfully submitted,

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